REMARKS

The Applicants appreciate the Examiner's time and efforts in granting interviews on May 8, 2006, May 11, 2006, May 19, 2006, and May 22, 2006. The Applicants and Examiner discussed the current state of the Office Action, the "monomer" limitation, which was not present in Lechuga, the unexpected sequestration of F.IX, and the inventive entities of current application.

The Examiner has withdrawn the enablement and indefiniteness rejections (35USC§112). The Examiner noted that "monomer" was a property of protein quaternary structure and that Lechuga did **not** disclose "monomeric" F.IX. The Examiner has maintained the obvious double-patenting rejection and a §103 obviousness rejection in light of Lechuga.

A. Lechuga does not disclose "monomeric" F.IX

The present application discloses and claims "monomeric" F.IX for the treatment of hemophilia. It also discloses the difficulty in generating a monomeric F.IX, the steps that must be taken to ensure "at least 90% monomeric" proteins are generated, and that lesser levels of monomeric protein are not active.

For example, Table 7a surprisingly demonstrates that monomer content below 80% was **inactive**, rather than merely less active as might be expected. Specifically, it shows that preparations with greater than 90% activity were active while preparation 13 with 80.7% monomer content could not be measured "n/a." Therefore, the data shows that without careful formulation, the F.IX can aggregate and that such aggregates are not active.

As admitted by the Examiner, Lechuga does **not** teach that protein must be monomeric, nor that it must be almost completely monomeric for activity.

Therefore, the prior art **fails to teach** the limitation of "monomer" or "at least 90% monomer," and the *prima facie* obviousness case is not met. Therefore, Applicants respectfully requests allowance.

B. Lechuga teaches away from "does not have ethanol"

Further, Lechuga teaches that ethanol can be used to prepare spray dried formulations (p. 17, ll. 19-20). However, ethanol spray-drying causes negative morphological changes in F.IX:

> (¶82) "In study 2, the ethanol and leucine formulations each had a 3% drop in monomer content comparing the pre-spray dried solution to the reconstituted aerosol drug powder at initial"
>
> (¶83) "The ethanol (lot 4) spray dried powder was the only formulation that demonstrated morphological changes as observed by SEM. At 2 weeks stability at 40°C/75% RH, the ethanol formulation was more wrinkled and contained fracture fragments. No significant morphology changes were noted on any of the other powders when exposed to identical storage conditions. This data suggests that dry F.IX suitable for pulmonary delivery should not be spray dried with alcohol."

Therefore, Lechuga **teaches away** from the invention as claimed (claims 4, 10, 17, 20, 24). Therefore, these claims (at least) are believed to be allowable and Applicants respectfully requests same.

C. Unexpected results – sequestration effect

The use of monomeric F.IX provides a sequestration effect. The application specifically states that monomeric F.IX is sequestered allowing for a bi-weekly treatment which lasts 2-4 days (¶22). Prior intravenous treatments were more rapidly cleared from the blood, thus a bi-weekly prophylactic treatment would not have been possible (Fig. 8).

The sequestration and prophylactic treatment using F.IX was not disclosed, nor predictable from the Lechuga reference.

The sequestration effect offered by monomeric F.IX is an **unexpected result** obtained with the present invention. Thus, even if the *prima facie* obviousness case were met (and it is not), claim 14 *et seq* recite the entirely unexpected result of being able to treat hemophilia "in advance" of a bleeding episode due to this surprising sequestration effect and the case is rebutted. Therefore, claims 14 *et seq* (at least) are believed to be allowable and Applicants respectfully requests same.

D. Statutorily distinct inventions

Because monomeric F.IX is not obvious, as demonstrated above, the obviousness-type double patenting rejection is moot. The prior applications (USSN 10/313,343 and USSN 10/313,961) do not disclose "monomeric" F.IX, teach active preparations of "at least 90%" monomeric F.IX, or disclose a prophylactic treatments "in advance" of bleeding episodes. Thus the present invention cannot be obvious, and Applicants respectfully request that the obvious-type double patenting rejection be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. The Applicants respectfully request the Examiner contact them if there are any questions or procedures that need to be addressed. No fees are believed to be due for this submission. However, should there be any additional fees required, please charge such additional fees to Deposit Account No. 50-3420 (reference 31175413-010002 MDB)

Dated: May 22, 2006

Respectfully submitted,

BAKER & MCKENZIE LLP

By /Michael D. Berger/

Michael D. Berger Ph.D., Patent Agent
Registration No.: 52,616
Pennzoil Place, South Tower
711 Louisiana, Suite 3400
Houston, Texas 77002-2746 USA
Tel: +1 713 427 5031
Fax: +1 713 427 5099
Attorneys For Applicants